Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/crvasa

Original research article – *Special issue: Acute Coronary Syndromes*

Trends in epidemiology and the treatment of acute coronary syndromes in the Czech Republic: Comparison of the CZECH-1 and CZECH-2 registries

Petr Toušek [a,*], *David Horák* [b], *František Toušek* [c], *Richard Rokyta* [d], *Pavel Červinka* [e], *Michael Želízko* [f], *Michael Aschermann* [h], *Petr Janský* [g], *František Holm* [b], *Ladislav Pešl* [c], *Jiří Jarkovský* [i], *Petr Widimský* [a] *on behalf of CZECH-1 and CZECH-2 Investigators* [1]

[a] *Cardiocenter, Third Faculty of Medicine, Charles University, Prague, Czech Republic*
[b] *Cardiocenter, Hospital Liberec, Liberec, Czech Republic*
[c] *Regional Hospital, Department of Cardiology, České Budějovice, Czech Republic*
[d] *University Hospital Plzeň, Faculty of Medicine Plzeň, Charles University, Department of Cardiology, Plzeň, Czech Republic*
[e] *Masaryk Hospital, Department of Cardiology, Ústí nad Labem, Czech Republic*
[f] *Department of Cardiology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic*
[g] *Cardiocenter, University Hospital Motol, Prague, Czech Republic*
[h] *Second Department of Internal Medicine, Cardiology and Angiology, General University Hospital, First Faculty of Medicine, Charles University, Prague, Czech Republic*
[i] *Masaryk University, Faculty of Medicine, Institute for Biostatistics and Analysis, Brno, Czech Republic*

ARTICLE INFO

Article history:
Received 5 March 2014
Received in revised form
27 May 2014
Accepted 18 June 2014
Available online 22 July 2014

Keywords:
Acute coronary syndrome
Epidemiology
Incidence
Treatment
Primary percutaneous coronary intervention

ABSTRACT

Background: The clinical spectrum of acute coronary syndrome (ACS) has changed due to a progressively ageing population over the last two decades.
Aim: We analysed the changes in the epidemiological and treatment strategies between two large registries that were performed in 2005 and 2012 in well-defined populations of the Czech Republic.
Methods and results: The CZECH-1 and CZECH-2 registries enrolled all consecutive hospitalized patients with an initial diagnosis of ACS during a 1 or 2-month period, respectively. Thirty-six and 32 hospitals participated in the CZECH-1 and CZECH-2 registries, respectively. A total of 1921 patients were enrolled in the CZECH-1 registry and 1221 patients participated in the CZECH-2 registry. Patients enrolled in the CZECH-2 registry were older than those in CZECH-1 (68 ± 12 vs. 66 ± 12 years; $p < 0.001$). ACS was not confirmed during hospitalization in 30.5 and 30.1% ($p > 0.05$) of the patients in the CZECH-1 and CZECH-2 registries, respectively. Urgent angiography in patients with ST segment elevation myocardial infarction (STEMI) was performed in 92 and 94% of the patients ($p > 0.05$), respectively; of these, 87 and 89% subsequently underwent primary PCI. There were no signifiant differences in in-hospital (4.2 vs. 4.4%, p=0.805) or in the mortality of patients with a final diagnosis of

* *Corresponding author at*: Cardiocenter, Charles University, Third Faculty of Medicine, Ruska 87, Prague 100 00, Czech Republic. Tel.: +420 267 162 621; fax: +420 267 162 525.
E-mail addresses: petr.tousek@fnkv.cz, tousek@email.cz, tousek.p@seznam.cz (P. Toušek).
[1] See Appendix A.
http://dx.doi.org/10.1016/j.crvasa.2014.06.006

Q-myocardial (10.3 vs. 10.7%; $p = 0.870$) or non-Q-myocardial infarction (4.7 vs. 3.8%; $p = 0.497$) between the two registries. The estimated incidence of confirmed ACS and STEMI in a representative population from both registries was 3248 and 661 cases/million individuals/year in the CZECH-1 registry and 2149 and 652 cases/million individuals/year in the CZECH-2 registry. The fall in ACS incidence was almost exclusively due to a significant decrease in the incidence of unstable angina as the final diagnosis. At discharge, the patients with confirmed ACS were administered the following medications: aspirin (95 vs. 94%; $p > 0.05$), clopidogrel (60 vs. 76.4%; $p < 0.001$), beta-blockers (78 vs. 78%; $p > 0.05$), angiotensin-converting enzyme (ACE) inhibitors (50 vs. 78%; $p = <0.001$) and statins (75 vs. 90%; $p < 0.001$) in the CZECH-1 and CZECH-2 registries, respectively.

Conclusion: In the Czech Republic, the age of the patients hospitalized with ACS increased between 2005 and 2012. Invasive reperfusion strategy for patients with STEMI was very high in both registries. The overall outcome in patients with confirmed ACS did not change between 2005 and 2012. The estimated incidence of ACS decreased due to the fall in unstable angina pectoris.

Introduction

For the last 15 years, there has been a well-established network of regional hospitals and tertiary centres with percutaneous coronary intervention (PCI) capability for managing the patients with acute coronary syndrome (ACS) in the Czech Republic. However, progressive population ageing has also occurred during this period, and consequently the characteristics of the patients admitted for ACS have changed [1–3]. Two large registries of unselected patients that were hospitalized with an initial diagnosis of ACS were performed in 2005 and 2012 in well-defined populations of the Czech Republic [4,5]. We analysed the changes in the epidemiological and treatment strategies used between the two registries, which were performed 7 years apart.

Methods

The CZECH-1 registry was performed from 1 to 30 November 2005 in all 21 cardiocentres (percutaneous coronary intervention [PCI] centres) open at the time in the Czech Republic. All regional community hospitals ($n = 15$) without catheterization availability in the two counties of the Czech Republic also participated. The CZECH-2 registry was performed in October and November 2012 in the four counties of the Czech Republic, encompassing 28 regional hospitals without catheterization availability and four cardiocentres with catheterization laboratories. The locations of the participating centres in both registries are shown in Fig. 1. All regional hospitals and two cardiocentres in South Bohemian and Liberec counties participated in both registries, covering a population of ~1 million inhabitants.

The inclusion criteria were the same for entry into both registries: hospital admission with a diagnosis of ST segment elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), unstable angina pectoris (UAP), acute heart failure in patients with known coronary artery disease (CAD), chest pain with suspected ACS, resuscitation in the prehospital phase or another initial diagnosis that was confirmed as ACS during hospitalization.

In-hospital mortality was evaluated in all the patients. The final diagnosis and confirmation or exclusion of ACS were performed according to the criteria for and definition of ACS.

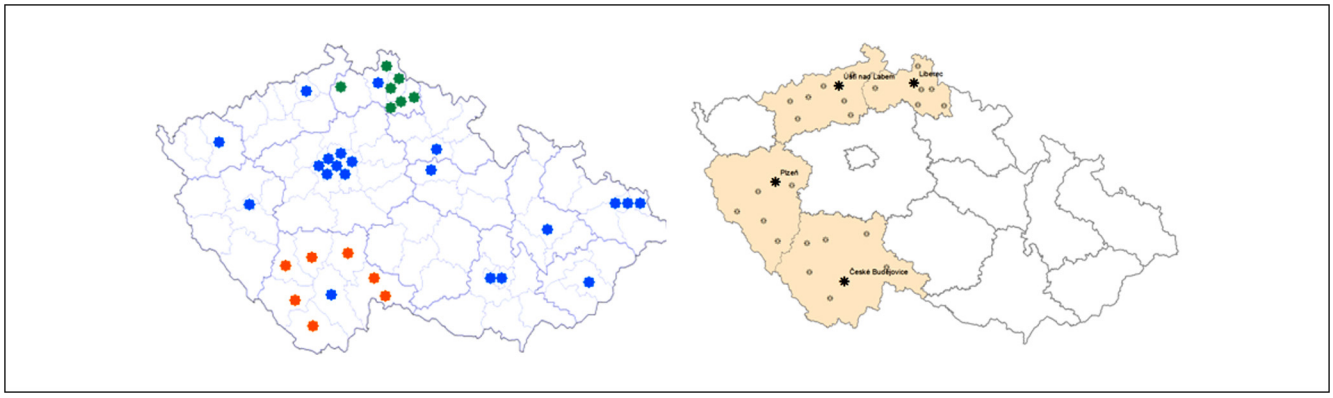

Fig. 1 – The location of the centres that participated in the CZECH-1 (left, 21 cardiocentres represented with blue asterisks) and CZECH-2 registries (4 cardiocentres represented by black asterisks). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

The definition of discharge Q wave myocardial infarction (Q-MI) was based on the development of new pathologic Q waves in two continuous leads on electrocardiography (ECG). The estimated incidence of confirmed ACS was based on the number of inhabitants in the representative area of the South Bohemian and Liberec counties that participated in both registries according to the Czech Statistical Office [1].

Standard descriptive statistics were applied to the analyses, including absolute and relative frequencies for categorical variables and means ± standard deviation for continuous variables. The statistical significance of differences among the groups of the patients was calculated using the maximum likelihood chi-squared test for categorical variables and analysis of variance (ANOVA) for continuous variables. The level of statistical significance was set at $p \leq 0.05$; SPSS 19 for Windows (version 19.0.1; IBM Corp., 2010) was used for the analysis.

Results

A total of 1921 and 1221 patients were enrolled in the CZECH-1 and CZECH-2 registries, respectively. There were 41.3 and 36.9% of the female subjects in the respective registries ($p = 0.027$). Patients in the CZECH-2 registry were older than those enrolled in CZECH-1 (68 ± 12 vs. 66 ± 12 years; $p < 0.001$). Additional clinical characteristics of the patients in both registries are shown in Table 1.

Diagnosis on admission

The major initial diagnosis in the CZECH-1 registry was UAP in 29% of the patients, whereas most patients in the CZECH-2 registry were admitted for chest pain thought to be due to ACS (36%). There were no significant differences in the percentage of the patients initially diagnosed with STEMI between the registries (24.3 vs. 22.1%, $p \geq 0.05$). Statistical differences were observed in the initial diagnosis of different types of ACS without ST elevation (NSTE-ACS). Patients in the CZECH-2 registry were also more frequently admitted for acute heart failure in the presence of CAD (2.1 vs. 9.1%; $p < 0.001$). The different initial diagnoses at admission are shown in Fig. 2.

Table 1 – Comparison of the clinical characteristics of the patients enrolled in the CZECH-1 and CZECH-2 registries.

Clinical characteristics		CZECH-1	CZECH-2	p
BMI (kg/m^2)	≤20	1.5%	1.6%	0.859
	20.1–25	21.9%	21.6%	
	25.1–3.0	43.2%	44.7%	
	≥30.1	32.3%	33.3%	
Smoking	Non-smoker	45.5%	43%	
	Active smoker	13.9%	26.7%	<0.001
	Ex-smoker	40.6%	30.3%	
Diabetes	Type 2	32.0%	34.4%	0.159
Dyslipidaemia		39.7%	47.6%	<0.001
Hypertension		69.3%	71.7%	0.281
Atrial fibrillation		13.0%	13.3%	0.814
History of	Stroke	10.7%	8.4%	0.031
	IM	26.9%	24.7%	0.168
	PCI	15.4%	20.4%	<0.001
	CABG	7.4%	9.6%	0.034

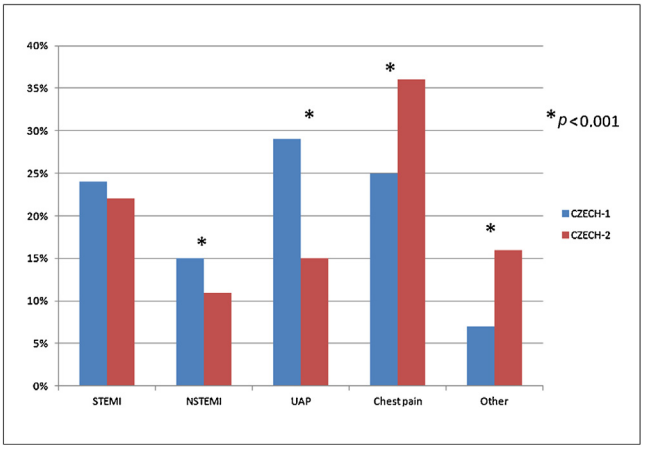

Fig. 2 – Initial diagnosis of the patients admitted to the CZECH-1 (blue bars) and CZECH-2 registries (red bars). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

Diagnosis at discharge

ACS was not confirmed during hospitalization in 30.5 and 30.1% ($p = 0.635$) of the patients in the CZECH-1 and CZECH-2 registries, respectively. The proportion of the patients in whom a different type of ACS was confirmed at discharge is shown in Fig. 3.

Reperfusion strategy in cases involving STEMI

Urgent angiography was performed in 92% of the patients in the CZECH-1 registry and in 94% of those in CZECH-2 ($p > 0.05$). The time interval (median) from the onset of chest pain to the first diagnostic ECG was 150 min (69–420 min for the 25–75th percentile) in the CZECH-1 registry, and 150 min (69–455 min

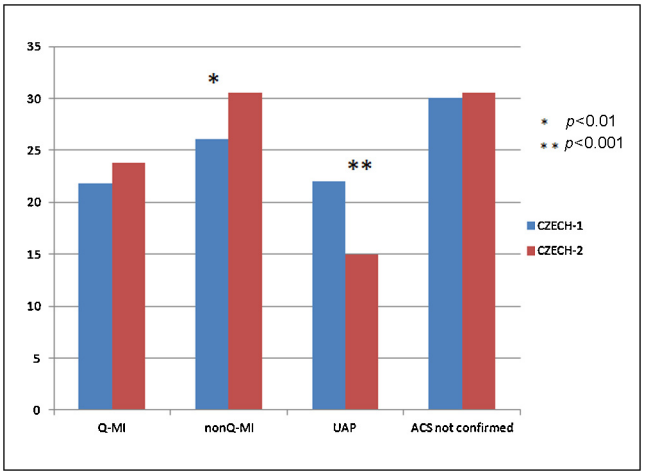

Fig. 3 – Final diagnosis in patients admitted to the CZECH-1 (blue bars) and CZECH-2 registries (red bars). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

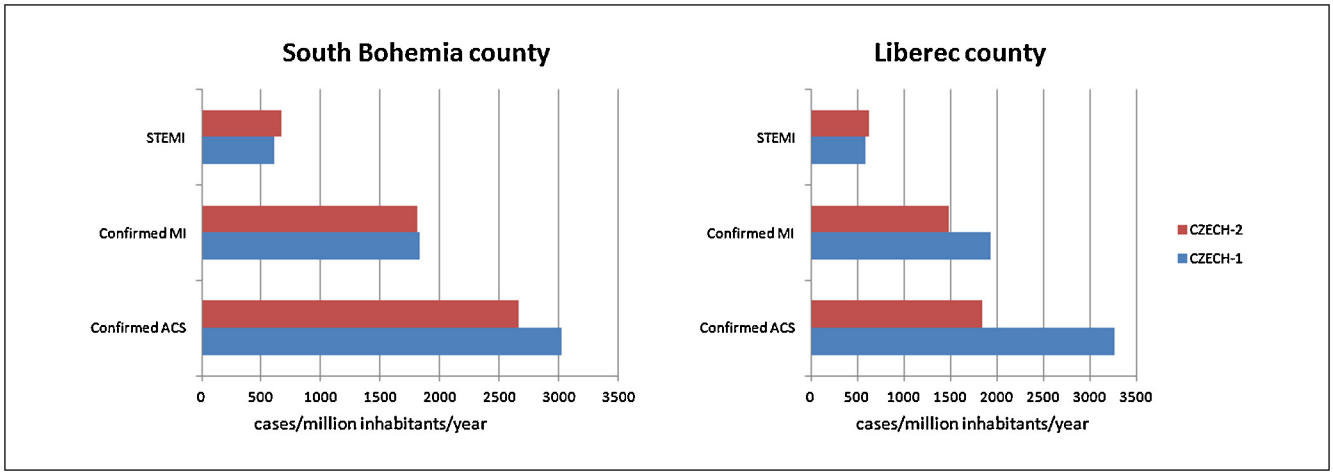

Fig. 4 – Differences in the estimated incidence of ACS between the CZECH-1 and CZECH-2 registries in South Bohemian and Liberec counties.

for the 25–75th percentile; $p = 0.399$) in CZECH-2. The median interval from ECG to catheterization in the two registries was 70 (60–180 min for the 25–75th percentile) and 85 min (58–128 min for the 25–75th percentile; $p = 0.289$), respectively.

Invasive treatment in the patients with ACS without ST elevation

Coronary angiography during hospitalization was performed in 85 and 65% of the patients with NSTEMI in the CZECH-1 and CZECH-2 registries, respectively ($p < 0.01$); of these, 75 and 71% of the patients underwent PCI ($p > 0.05$), and 18 and 17% underwent a coronary artery bypass graft (CABG). Coronary angiography was performed in 72 and 66% of the patients with UAP in the CZECH-1 and CZECH-2 registries, respectively ($p < 0.05$); this was followed by PCI in 58 and 61% of the patients ($p > 0.05$). Differences in the indications for coronary angiography during hospitalization were observed between the cardiocentres with PCI capability and the regional hospitals (94 vs. 55% for NSTEMI [$p < 0.001$] and 98 vs. 52% for UAP [$p < 0.001$], respectively).

Mortality

The in-hospital mortality rates in the entire CZECH-1 and CZECH-2 populations were 4.4 and 4.2% ($p = 0.805$), respectively. In patients with confirmed myocardial infarction (MI) according to the development of pathological Q waves on ECG at discharge, the in-hospital mortality rates were 4.7 and 3.8% ($p = 0.497$) for non-Q-IM, and 10.3 and 10.7% ($p = 0.870$) for Q-IM. The in-hospital mortality of the patients with STEMI treated by primary PCI in the CZECH-1 and CZECH-2 registries was 5.5 and 5.1% ($p = 0.625$), respectively. The in-hospital mortality and 30-day mortality of all the patients with STEMI in the CZECH-2 registry were 6.1 and 7.3%, respectively.

Pharmacological treatment

In the patients with confirmed ACS, the following medications were administered in the CZECH-1 and CZECH-2 registries at discharge: aspirin (95 vs. 94%; p = NS), clopidogrel (60 vs. 76.4%; $p < 0.001$), beta-blockers (78 vs. 78%; $p > 0.05$), angiotensin-converting enzyme (ACE) inhibitors (50 vs. 78%; $p < 0.001$) and statins (75 vs. 90%; $p < 0.001$).

Incidence

The estimated incidence of confirmed ACS based on the number of inhabitants living in the two counties of the Czech Republic that participated in the CZECH-1 and -2 registries was 3248 and 2149 cases/million inhabitants/year, respectively. The estimated incidence of confirmed MI in the CZECH-1 and -2 registries was 1960 and 1680 cases/million inhabitants/year, whereas the estimated incidence of STEMI was 661 and 652 cases/million inhabitants/year, respectively. Differences in the estimated incidence of ACS between the registries in the two counties are shown in Fig. 4. A similar estimated incidence of STEMI was observed in both registries and counties; however, differences in the estimated incidence of NSTEMI and UAP were observed.

Discussion

This study compared two large registries that were performed in the Czech Republic at a 7-year interval; both studies enrolled patients with an initial diagnosis of ACS. Although a different number of regional and tertiary hospitals participated in the CZECH-1 and CZECH-2 registries, both had the same inclusion criteria in terms of an initial diagnosis of ACS, and both enrolled all hospitalized patients within a defined period. Furthermore, all hospitals in the two counties (South Bohemian and Liberec) of the Czech Republic, covering a population of ~1 million inhabitants, participated in both registries. Therefore, this comparison has the potential to identify the trends in the epidemiology and treatment of unselected populations with an initial diagnosis of ACS.

When the basic clinical characteristics of the patients were compared between the registries, there was a higher mean age of the patients in the CZECH-2 registry. This difference was

mainly caused by a decreased number of hospitalized patients aged 40–60 years (29.8 vs. 23.0%) and an increased number of octogenarians (11.2 vs. 19.2%). An increasing number of patients with previous revascularization were also hospitalized with the suspicion of ACS. Surprisingly, more patients in the CZECH-2 registry were also active smokers.

ACS was excluded in 30% of the admitted patients in both registries. Only a small number of previous registries have included data from unselected patients admitted with the suspicion of ACS. In the Global Registry of Acute Coronary Events (GRACE) and Canadian Registry of Acute Coronary Events (CANRACE) registries, 14% of the patients did not have a final diagnosis of ACS [6]. However, the inclusion criteria for these registries differed from those in the current study, because at least one positive biomarker, ECG changes or a documented history of coronary artery disease, was required for inclusion. Therefore, because determining the appropriate diagnoses is challenging, it is clear that a high proportion of the patients are still admitted with possible ACS during clinical practice, in whom ACS is later excluded.

Most patients with STEMI in both the CZECH-1 and CZECH-2 registries underwent urgent angiography with primary PCI. The Czech Republic has one of the highest percentages of the patients with STEMI who undergo primary PCI and numbers of primary PCI per million inhabitants among the European countries [7,8]. Approximately 25% of the patients with STEMI presented to a regional hospital; emergency medical personnel then directly referred most of these to a cardiocentre. This shows good organization of the emergency network when handling patients diagnosed with STEMI. Longer time interval from ECG to catheterization laboratory in the CZECH-2 registry can be explained by the different proportions of regional hospitals and cardiocentres in both registries with longer transport distances in the CZECH-2 registry.

The main limitation of this study is the different proportions of regional hospitals and cardiocentres that participated in the CZECH-1 and -2 registries. In the CZECH-1 registry, cardiocentres dominated in participation. This might influence comparisons of the clinical characteristics and treatment strategies in patients with ACS without ST elevation. Patients admitted at a regional hospital for NSTEMI and UAP were significantly older and had more comorbidities than did patients admitted to a cardiocentre. Differences in the indications for coronary angiography in patients with NSTEMI and UAP during hospitalization were also clearly observed between the cardiocentres with PCI capability and regional hospitals. This could be explained by the following factors: first, ~20% of the patients admitted to regional hospitals undergo coronary angiography electively after discharge; second, 12.7% of the patients in the CZECH-2 registry refused to be transferred from a regional hospital to a PCI centre; and third, patients with NSTE-ACS had several comorbidities and were considered unsuitable for transfer to a PCI centre by the physicians at regional hospitals. A similar approach for the invasive management of the patients with NSTE-ACS admitted to non-PCI centres was seen in the Acute coronary syndromes – Longitudinal Evaluation of Real-life Treatment in non-PCI hospitals in the Czech Republic (ALERT-CZ) registry [9]. In ALERT-CZ, coronary angiography was performed during the initial hospitalization or later in 72.5% of the 4625 patients with non-NSTE-ACS. Another limitation of the current study is the relatively short period of data collection in both the CZECH-1 (1 month) and -2 registries (2 months). Therefore, the reported annual incidence of ACS must be regarded as an estimated incidence. This might partially explain the different incidences of ACS in Liberec County between 2005 and 2012. In addition, the difference in the estimated incidence of ACS among the counties is caused mainly by a decreased number of admitted patients with a final diagnosis of UAP. Therefore, it is possible that more patients presenting with chest pain but without positive cardiac markers and ECG changes were not admitted during the CZECH-2 registry.

Despite the differences in the clinical characteristics and invasive approaches to NSTE-ACS between the CZECH-1 and -2 registries, the in-hospital mortality of all the patients and the definitive diagnosis of Q-MI or non-Q-MI remained consistent. Furthermore, there was a trend for greater use of recommended evidence-based medication at discharge in patients with confirmed ACS.

Conflict of interest

All authors disclose any actual or potential conflict of interest.

Funding body

The Czech Society of Cardiology organized the CZECH-1 registry and the Third Faculty of Medicine, Charles University, Prague arranged the CZECH-2 registry. Sanofi-Aventis (CZECH-1), AstraZeneca Czech Republic (CZECH-2), and České Budějovice Cardiocenter Foundation supported the registries financially.

Ethical statement

Hereby we state that the research was done according to the ethical standards.

Appendix A. CZECH-1 and CZECH-2 Investigators

CZECH-1 registry

PCI centers: Michael Aschermann, Jana Bednářová, Pavel Boček, Marian Branny, Zdeněk Coufal, Petr Hájek, Marcel Heczilo, Jiří Herman, František Holm, Ivo Horák, Ivan Horníček, Petr Janský, Pavel Jelínek, Petr Kala, Bohdan Kallmunzer, Vladimír Karmazín, Vladimír Kaučák, Ludmila Klemsová, Aleš Kovářík, Radim Krýza, Jana Kupčíková, Martin Malý, Jan Matějka, Jana Matoušková, Jan Mrozek, Dita Nováková, Kamil Novobilský, Marcela Olšová, Pavel Osmančík, Jiří Ostřanský, Renata Pavelková, Silva Rajecká, Čestmír Ramík, Milan Ranostaj, Marek Richter, Pavel Sedloň, Martin Slabák, Martin Sluka, Vladimír Srp, Zdeněk Šembera, Hana Štěpničková, Peter Telekes, František Toušek, Jan Vojáček, Petr Widimský, Jana Zarembová, Eva Zvolánková, Jaroslav Žák, and Michael Želízko.

Regional hospitals: Dušan Astl, Romana Balková, Lubomír Ballek, Věra Cempírková, Jana Davídková, Ladislav Fábik, Pavel Hausdorf, Pavel Havránek, Zdeněk Holý, Oldřich Honců, Jindřich Charouzek, Jiří Jalůvka, Al-haj Khaled, Silvia Krajíčková, Ivana Křížová, Pavel Lipták, Bohdan Lukáč, Marek Míka, Karol Odzgan, Eva Pauchová, Pavel Plecháč, Jiří Plocek, Josef Pola, Pavel Sábl, Martin Schmoranz, Richard Stoupenec, Vladana Strašlipková, Jana Svobodová, Martina Šteflová, Angela Škarýdová, Ivan Švihálek, Jiří Tomášek, Soňa Trachtová, Zdeněk Velička, and Tomáš Velimský.

CZECH-2 registy

Lubomír Ballek, Ondřej Beneš, Pavel Červinka, Jiří Dostál, Antonín Egert, Jindřich Florián, Pavel Hausdorf, Jana Havelková, Jiří Herman, Zdeněk Holý, Oldřich Honců, Michal Hondl, Oldřich Honsnejman, David Horák, David Gerber, Jana Junková, Martina Kalová, Milada Kladívková, Jitka Kobrlová, Rudolf Koubek, Monika Kunová, Bohdan Lukáč, Marek Mika, Jana Mikulová, Jiří Malý, Zuzana Neužilová, Vratislav Pechman, Ladislav Pešl, Josef Pola, Hana Polívková, Pavla Průšová, Petr Reichert, Lenka Roblová, Richard Rokyta, Aleš Sedláček, Martin Straka, Marta Šifaldová, Jakub Tocháček, František Toušek, Petr Toušek, Roman Tytl, and Petr Widimský.

REFERENCES

[1] http://www.czso.cz/eng/redakce.nsf/i/home.

[2] R.W. Yeh, S. Sidney, M. Chandra, et al., Population trends in the incidence and outcomes of acute myocardial infarction, The New England Journal of Medicine 362 (23) (2010) 2155–2165.

[3] E. Puymirat, T. Simon, P.G. Steg, et al., Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction, The Journal of the American Medical Association 308 (10) (2012) 998–1006.

[4] P. Widimsky, M. Zelizko, P. Jansky, et al., The incidence, treatment strategies and outcomes of acute coronary syndromes in the ''reperfusion network'' of different hospital types in the Czech Republic: results of the Czech evaluation of acute coronary syndromes in hospitalized patients (CZECH) registry, International Journal of Cardiology 119 (2) (2007) 212–219.

[5] P. Tousek, F. Tousek, D. Horak, et al., The incidence and outcomes of acute coronary syndromes in a central European country: results of the CZECH-2 registry, International Journal of Cardiology 173 (2) (2014) 204–208.

[6] R.R. Bajaj, S.G. Goodman, R.T. Yan, et al., Treatment and outcomes of patients with suspected acute coronary syndromes in relation to initial diagnostic impressions (insights from the Canadian Global Registry of Acute Coronary Events [GRACE] and Canadian Registry of Acute Coronary Events [CANRACE]), The American Journal of Cardiology 111 (2) (2013) 202–207.

[7] P. Widimsky, W. Wijns, J. Fajadet, et al., Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries, European Heart Journal 31 (8) (2010) 943–957.

[8] S.D. Kristensen, K.G. Laut, J. Fajadet, et al., Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries, European Heart Journal (2014) (Epub ahead of print).

[9] P. Widimský, J. Zvárová, Z. Monhart, et al., The use of revascularization strategies in patients with acute coronary syndromes admitted to hospitals without catheterization facilities: results from the ALERT-CZ registry, Cor et Vasa 55 (3) (2013) e207–e211.